

Summary of the Invention

5 It is an object of the present invention to provide a system for delivering a shear-sensitive injectable material. As defined herein, a "shear-sensitive injectable material" is a material which comprises components, or is itself a component, which is subject to shear (e.g., causing degradation or a change in viscosity) upon mixing and passage through a standard-sized needle (e.g., about 10 gauge to about 25 gauge). In the process of mixing, shear-sensitive injectable
10 materials form paste-like compounds which are ideal for implantation into the body because they conserve their volume and do not migrate far from a site of injection. Such materials are useful in applications to bulk-up, augment, or replace tissues.

The present invention relates to a delivery system for delivering a shear-sensitive injectable material into the body of a mammal, such as a human being. The delivery system acts
15 as a mechanical feed which continuously mixes a shear-sensitive injectable material as it delivers the shear-sensitive injectable material to a target tissue, or to a site adjacent a target tissue, within the body of a mammal. In one embodiment of the invention, the delivery system is composed of an injector system having a rotatable mixing member coupled to a driving system.

The injector system comprises an injector housing defining a lumen and having an output
20 end coupled to a needle assembly for coupling to a needle and a driving system connection end for coupling to a drive mechanism. A mixing member extends within the lumen of the injector housing from the driving system connection end of the housing to at least the output end, and is rotatable within the lumen to feed the shear-sensitive injectable material out through the output end through the needle assembly. In a further embodiment of the invention, the injector housing
25 comprises a feeder and a reservoir; the reservoir coupled at one end to the feeder and at the other end to a needle assembly. In this embodiment, the mixing member rotates within the feeder to feed a shear sensitive injectable material into the reservoir and moves linearly within the reservoir portion to push the shear-sensitive injectable material through the needle assembly.

A driving system is provided for use with the injector system. The driving system
30 includes a drive mechanism in communication with an actuator which is capable of actuating the

drive mechanism. An interfacing member is coupled to the drive mechanism and is for coupling to the mixing member of the injector system. In operation, the driving system is coupled to the injector system via the interfacing member. Actuation of the drive mechanism causes the mixing member to rotate within the lumen of the injector housing, thereby to mix and deliver a shear-sensitive injectable material within the injector housing through the output end of the injector housing to an injection site. In one embodiment of the invention the actuator comprises a switch and is coupled to an energy source, such as a battery, which is in electrical communication with the drive mechanism.

In another embodiment of the invention, the injector system is loaded with a shear-sensitive injectable material and is provided within a packaging to maintain the sterility of the injector system. In this embodiment, the injector system is ready to be coupled to the drive mechanism of the driving system and to be injected into the body of a mammal.

In yet another embodiment of the invention, a coupling system is provided for coupling to a tube of a syringe. The coupling system adapts the tube of the syringe to deliver a shear-sensitive injectable material into the body of a mammal. The coupling system has a coupling housing capable of mating with the tube of the syringe. A drive mechanism is positioned within the coupling housing and is capable of providing a rotary force upon actuation by the user. The coupling system also includes a mixing member which is for coupling to the drive mechanism and which extends within the tube of the syringe when the coupling housing is mated to the tube of the syringe. Upon actuation of the drive mechanism, the mixing member rotates in response to rotary force from the drive mechanism. The rotation of the mixing member simultaneously mixes and delivers a shear-sensitive injectable material loaded within the syringe. In some embodiments of the invention, the coupling housing further comprises an actuator for actuating the drive mechanism. In yet other embodiments of the invention, the coupling housing comprises finger grips for ease of manipulation of the housing and tube of the syringe during the injection process.

Brief Description of the Drawings

In the drawings, like reference characters generally refer to the same parts throughout the different views. Also, the drawings are not necessarily to scale, emphasis instead generally being placed upon illustrating the principles of the invention.

Figure 1 shows one embodiment of a delivery system according to the invention wherein the drive system features finger grips for ease of manipulation.

Figure 2 is a schematic longitudinal view of one embodiment of an injector system according to the invention.

Figures 3A-3E show views of mixing members according to the invention. Figure 3A shows a mixing member having variably spaced threads and a constant outer diameter. Figure 3B shows a mixing member having uniformly spaced threads and a varying outer diameter. Figure 3C shows a mixing member having both variably spaced threads and a varying outer diameter. Figure 3D shows a mixing member having a constant outer diameter and multiple starts. Figure 3E shows a mixing member having threads with a varying radial height and a constant outer diameter.

Figure 4 shows one embodiment of a drive system according to the invention.

Figure 5 shows one embodiment of a coupling system according to the invention.

Figures 6A-B show an embodiment of a delivery system which is capable of operating in both a feed mode and a plunger mode. Figure 6A shows the device operating in a feed mode. Figure 6B shows the device operating in a plunger mode.

Description

Referring to Figure 1, the delivery system 1 may be used for delivering a shear-sensitive injectable material 13 into the body of a mammal. The delivery system 1 acts as a mechanical feed to mix continuously a shear-sensitive injectable material 13 as it is delivered to a tissue or to

a site adjacent to a tissue within the body of a mammal. The delivery system 1 comprises an injector system 9 (shown alone in Figure 2) and a driving system 19 (shown alone in Figure 4).

In one embodiment of the invention, and referring to Figure 2, the injector system 9 comprises an injector housing 7 defining a lumen 7L and having an output end 16 and a driving system connection end 17. A mixing member 10 extends within the lumen 7L of the injector housing 7 from the driving system connection end 17 to at least the output end 16. The mixing member 10 rotates within the lumen 7L to mix and deliver an injectable 13 into the body of a mammal. Rotation of the mixing member causes a shear-sensitive injectable material within the lumen 7L to move forward to the output end 16 causing ejection of the shear-sensitive material through the output end 16. The output end 16 has a smaller inner diameter than the lumen 7L of the of the injector system 9.

In one embodiment of the invention, the mixing member 10 is in the form of an elongated helical element. Helical elements encompassed within the scope of the present invention include, but are not limited to, augers, screws, corkscrews, and impellers. In one embodiment, shown in Figures 3A-3C, the helical element is a screw 10s with a substantially conical shape which tapers in the direction of transport of the shear-sensitive injectable material 13. In a further embodiment of the invention, the screw 10s comprises threads 10t. The design of the threads 10t can be optimized to reduce erosion on the surface of the thread 10t resulting from contact with the matrix materials within the shear-sensitive injectable material 13 (e.g., by providing rounded, polished ridges).

The outer diameter (OD) of the screw 10s and pitch of its threads 10t can take multiple forms depending on the delivery requirements (e.g., shear-sensitive injectable material 13 with more matrix material requires more pressure to deliver). A helical element with a larger OD will allow increased pressure to be exerted on the shear-sensitive injectable material 13; however, this is counterbalanced by increased back-pressure from the shear sensitive injectable material 13, especially at the output end 16 of the injector system 9. In one embodiment of the invention (not shown) the OD of the screw 10s approaches the diameter of the lumen 7L. In another embodiment, shown in Figure 3B, a screw 10s is provided having an OD which gradually decreases from the driving system connection end 17 to the output end 16 of the device, having an OD which is just slightly smaller than the diameter of the lumen 7L proximal to the driving

system connection end 17. This design prevents excessive pressure on the shear-sensitive injectable material 13 at the output end 16. A similar effect may be achieved by continuously increasing the pitch of the screw 10s from the driving system connection end 17 to the output end 16 (as shown in Figure 3B). In another embodiment of the invention, shown in Figure 3C, both the OD and pitch of the screw 10s are varied at the same time.

The threads 10t of the screw 10s provide channels through which the shear-sensitive injectable material 13 can flow and enhances mixing of the shear-sensitive injectable material 13 as the screw 10s rotates. The design and number of starts of the threads 10t can be varied to maximize mixing. In one embodiment, the radial height h of the threads 10t (i.e., from the base of the thread to its peak) is designed to be smallest at the driving system connection end 17 and greatest at the output end 16 to accommodate a higher proportion of unmixed matrix materials at the driving system connection end 17. The number of starts of the helical element may also be varied. In one embodiment of the invention, the threads 10t of the helical element comprise a single start (as in Figures 3A-3C, and 3E). In another embodiment of the invention, as shown in Figure 3D, the threads 10t of helical element comprise multiple starts.

The mixing member 10 is positioned within the lumen 7L of the injector housing 7 by a driver guide 11. The driver guide 11 is located proximal to the driving system connection end 17 of the injector housing 7 and is held in place by a rubber stopper 6 when the injector 9 is not in use (i.e., when the mixing member 10 is not rotating). The driver guide 11 permits rotational motion of the mixing member 10, but constrains lateral motion. When the injector system 9 is in operation, the stopper 6 and driver guide 11 move downward (i.e., in the direction of the output end 16) in the direction of flow of the shear-sensitive injectable material 13. The rotational motion of the mixing member 10, and the downward movement of the stopper 6 and driver guide 11, displaces the shear-sensitive injectable material 13 within the lumen 7L and ejects it out the output end 16. The rubber stopper 6 also maintains a seal between the driver guide 11 and the inner wall of the injector housing 7, preventing leakage of the shear-sensitive injectable material 13 at the driving system connection end 17. In a further embodiment, of the invention, the injector housing 7 is marked by indices (e.g., lines or tick marks indicating units of measurement such as "cc", "ml", or "oz.") allowing the user to monitor the amount of shear-sensitive injectable material 13 being delivered.

The injector system 9 further comprises a needle assembly 18 which may be an integral part of the injector housing 7, or which may be insert-molded onto an end 7d of the injector housing 7 distal to the motor connection end 17. The needle assembly 18 further comprises a needle 8 which may be an integral part of the needle assembly 18 or may be fitted onto the end 18e of the needle assembly 18 (e.g., by screwing onto threads fabricated at the end 18e of the needle assembly 18 or by luer lock). In this embodiment of the invention, standard needles 8 used in the art may be coupled to the end 18e of the needle assembly 18. In one embodiment of the invention, the distal end of the needle 8 is reduced in diameter to allow for a constant cross-sectional area through which to deliver or feed shear-sensitive injectable material 13. The diameter of the needle 8 should be small enough to permit injection into, or adjacent to, a target site within the body (e.g., about 10 gauge to about 25 gauge).

Shear-sensitive injectable material 13 can be used to bulk-up, augment, or replace a tissue. In one embodiment, the shear-sensitive injectable material 13 is a paste-like compound comprising a crosslinked material, a carrier, and a matrix material. Suitable crosslinked materials include, but are not limited to, collagen, polymers or copolymers of acrylonitrile, vinyl acetate, methacrylate, alginates, hydrogels, polyvinylpyrrolidone, hyaluronic acid, fibrin, polygalacturonic acid, propylene glycol alginic acid, polyarabinic acids, gum capparageen, polyphosphazenes, block copolymers such as polyethylene oxide-polypropylene glycol blocks, and combinations thereof. Crosslinking may be performed by exposing a crosslinkable material to changes in temperature, pH, or radiation. Chemical agents (non-ionic and ionic crosslinking agents) may also be used.

Suitable carrier materials are generally hydrophobic, and include, but are not limited to, oil, liquid polymers, liquid surfactants, and liquid plasticizers. Suitable matrix materials include, but are not limited to, fiber, chopped suture material, textured yarn material, ground suture material, ground fabric, polyester material, polytetrafluoride beads, silicon particles, polytetrafluoroethylene (PTFE) particles, ceramic particles, carbide particles, and combinations thereof. In embodiments where particles are used, particle diameters range from about 50 to about 250 microns. Ideal shear-sensitive injectable materials 13 are injectable, do not migrate a substantial distance from the injection site, and conserve their volume.

In another embodiment of the invention, bioactive materials may be additionally included with the shear-sensitive injectable material 13, such as proteins (e.g., growth factors, antibodies, ligands, receptors), naked or encapsulated nucleic acids (e.g., DNA, RNA, PNA molecules, aptamers, antisense molecules, and ribozymes), drugs, therapeutic agents, and the like. In a further embodiment of the invention, the shear-sensitive injectable material 13 is a material which may be injected into the body of mammal (e.g., a rabbit) to stimulate an immune response, i.e., such as polyacrylamide. In certain embodiments of the invention, the shear-sensitive injectable material 13 further comprises proteins, protein fragments, polypeptides (natural or synthetic), antigens, and the like.

In one embodiment of the invention, the injector system 9 is loaded with the shear-sensitive injectable material 13 and is provided within a packaging to maintain the sterility of the injector system 9. In this embodiment, the injector system 9 is ready to be coupled to the driving system 19 and the shear-sensitive injectable material 13 is ready to be injected into the body of a mammal. In general, the housing 7 of the injector system 9, including the needle assembly 18, with, or without the needle 8, is made of a material that is able to withstand conditions needed to sterilize or decontaminate it (e.g., autoclaving, irradiation, and/or exposure to chemical agents and/or anti-microbial agents) and is biocompatible. Suitable housing 7 materials include polypropylene, plastic, Teflon[®] material, PVC, and the like.

In a one embodiment of the invention, shown in Figure 4, a driving system 19 is provided for use in connection with the injector system 9. The driving system 19 comprises a drive mechanism 3 in communication with an actuator 15 which is capable of actuating the drive mechanism 3. An interfacing member 12 is coupled to the drive mechanism 3 and is for coupling to the mixing member 10 of the injector system 9.

In operation, as shown in Figure 1, the drive mechanism 3 is coupled to the injector system 9 via the interfacing member 12. In this embodiment of the invention, the delivery system 1 acts entirely in a "feed mode." Actuation of the drive mechanism 3 by the actuator 15 causes the mixing member 10 to rotate within the lumen 7L of the injector housing 7, thereby to mix and feed the shear-sensitive injectable material 13 disposed within the injector housing 7 through the output end 16 to an injection site (e.g., via the needle assembly).

In another embodiment of the invention, and referring to Figures 1, 4, and 5, the drive mechanism 3 is a motor which is contained within a motor housing 13 and includes a shaft 23 which is adapted for coupling to the interfacing member 12. In this embodiment of the invention, mechanical rotary force from the shaft 23 is transmitted through the interfacing member 12 to the mixing member 10, thereby rotating the mixing member 10 within the lumen 7L of the injector 9.

In one embodiment of the invention, shown in Figure 4, the drive mechanism 3 comprises an electric motor 20 which includes a conducting loop 22 mounted on a shaft 23 made of insulating material. A magnetic field around the loop 22, supplied by a magnet 21, causes the loop 22 to rotate when a current flows through it. The loop 22 causes the shaft 23 to rotate, transmitting rotary force to the mixing member 10 via the interfacing member 12. In another embodiment of the invention, the electric motor 20 is a DC motor and further comprises a commutator (not shown) for switching the direction of an electric current to maintain the shaft 23's direction of motion. In another embodiment of the invention, the drive mechanism 3 comprises a stationary loop 22 and a movable magnet 21. In a further embodiment of the invention, the motor 20 is a high torque low speed DC motor controlled by a switch.

The drive mechanism 3 may further include electrical connection elements 24 for connecting the motor 20 to an energy source 2, such as a battery. In one embodiment of the invention, shown in Figure 4, the flow of energy (e.g., current) from the energy source 2 is controlled by an actuator 15 to which it is coupled by electrical elements 15c. In a further embodiment of the invention, the actuator 15 comprises a switch which can be turned on and off by an operator.

In another embodiment of the invention, shown in Figures 6A-B, the delivery system 1 may be operated in both a feed mode and a "plunger mode." In this embodiment, the housing of the injector system defines a feeder 7f and a reservoir 7r. The reservoir 7r has a proximal end 27p and a distal end 27d. The proximal end 27p of the reservoir 7r is coupled to the end of feeder 7f distal from the driving system connection end 17 while the distal end 27d of the reservoir is coupled to the needle assembly 18. In one embodiment of the invention, the feeder 7f and reservoir 7p comprise a single unit molded together, while in another embodiment of the invention, the reservoir 7r is a module which can be separated from the feeder 7f.

During the feed mode of operation, shown in Figure 6A, the tip **10tp** of the mixing member **10** terminates within the feed portion **7f** of the delivery system **1**. Rotation of the mixing member **10** within the feed portion **7f** by the drive mechanism **3** then feeds the shear-sensitive injectable material **13** into the reservoir portion **7r** of the delivery system **1**. During the
 5 plunger mode of operation, shown in Figure 6B, a linear force is exerted on the mixing member **10**, either manually, mechanically, or through the use of the drive mechanism **3**, and the mixing member **10** is used as a plunger to push shear-sensitive injectable material **13** within the reservoir **7r** through the needle assembly **18**. This embodiment of the invention allows more force to be developed at the needle assembly **18** portion of the device, making it easier to inject the shear-
 10 sensitive injectable material **13** into a target tissue.

In a further embodiment of the invention, shown in Figure 5, a coupling system **25** is provided for coupling to a tube of a syringe. The coupling system **25** is for adapting the tube of the syringe to deliver a shear-sensitive injectable material **13** into the body of a mammal. The coupling system **25** comprises a coupling housing **26** capable of mating with the tube of the
 15 syringe at mating portion **4** of the coupling housing **26** (e.g., by a twisting and locking motion). A drive mechanism **3** is positioned within the coupling housing **26** and is capable of providing a rotary force upon actuation. The coupling system **25** also includes mixing member **10** which is for coupling to the drive mechanism **3** via interfacing member **12** and which extends within the tube of the syringe when the coupling housing **26** is mated to the tube of the syringe.

20 Upon actuation of the drive mechanism **3**, the mixing member **10** rotates in response to force from the drive mechanism **3**. The rotation of the mixing member **10** within the lumen **7L** simultaneously mixes and delivers a shear-sensitive injectable material **13** loaded within the tube of the syringe. In another embodiment of the invention, the coupling housing **26** further comprises an actuator **15** for actuating the drive mechanism **3**.

25 It should be apparent to those of skill in the art that the exact configuration of the housing **26** may be modified in many ways without affecting the operation of the coupling system **25**. In one embodiment of the invention, the coupling housing **26** comprises finger grips **5** for ease of manipulation of the coupling system **25** and syringe during the injection procedure, and can be manipulated with one or both hands. In another embodiment of the invention, a high torque low
 30 speed DC torque motor **20** is provided within the coupling housing **26**. The motor **20** is

actuatable by a switch that an operator can easily manipulate with a thumb while gripping the outside of the coupling housing 26. The intent is to provide an ergonomic feel to the user so that he or she may have or perceive control of the flow rate of material 13 exiting the syringe.

Although the mixing member 10 is shown coupled to the interfacing member 12 in Figures 5, 6A and 6B, the various components of the coupling system 25 may be provided separately, i.e., in the form of a kit, which may optionally include the tube of a syringe. The tube of the syringe may further be provided in a sterile or sterilizable packaging. In another embodiment of the invention, the mixing member 10 may be provided as part of the injector system 9, and may additionally include the shear-sensitive injectable material 13. Any of the injector system 9, or injector system 9 with shear-sensitive injectable material 13, may also be provided within a sterile or sterilizable packaging.

The coupling system 25 of the present invention may be adapted for coupling to a variety of standard sized syringes known in the art, from 1 cc to 50 cc. In one embodiment of the invention, the coupling system 25 is adapted for coupling to the injector system 9 discussed above, which may also be molded to a variety of sizes, and which may include indicia against which to measure the amount of shear-sensitive injectable material 13 being delivered (e.g., markings indicating "ml," "cc," or "oz." When injecting a shear-sensitive injectable material 13 to bulk-up, augment or replace tissue, a syringe or injector system 9 is selected which is capable of delivering an amount of shear-sensitive injectable material 13 suitable for a desired medical procedure. For example, the amount of material used for augmentation of anal sphincters is generally from 14-40 cc, and typically from about 20-30 cc, while the amount of shear-sensitive injectable material 13 that is used for muscle repair is typically from about 5 to about 10 cc.

Although the delivery system 1 of the present invention is particularly suited for the delivery of a shear-sensitive injectable material 13, because of its ability to act as a mechanical feed, it should be readily apparent to those of skill in the art, that the system may be used to deliver a variety of injectable materials, including fluids, to a target site.

Having thus described certain embodiments of the present invention, various alterations, modifications, and improvements will be apparent to those skilled in the art. Such variations, modifications, and improvements are intended to be within the spirit and scope of the invention.

The materials employed, as well as their shapes and dimensions, generally can vary. Accordingly, the foregoing description is by way of example only and is not intended to be limiting.

5 What is claimed is: